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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/800,077	03/12/2004	Ramachandra Reddy	VASG-P01-001	2078

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CHONG, KIMBERLY	
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1635	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/800,077	REDDY ET AL.	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7-11,14,16,18-25,59,61,62,65-81,92 and 93* is/are pending in the application.

4a) Of the above claim(s) *18-25,61,62 and 65-81* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7-11,16,59,92 and 93* is/are rejected.

7)☒ Claim(s) *14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 10/20/2008 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 07/22/2008 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 10/20/2008, claims 1, 5, 7-11, 14, 16, 18-25, 59, 61-62, 65-81 and new claims 92-93 are pending, claims 1, 5, 7-11, 14, 16, 59, 92 and 93 are currently under examination, claims 2-4, 6, 12-13, 15, 17, 26-29, 30-58, 60, 63-64 and 82-91 have been canceled and claims 18-25, 61-62, and 65-81 are withdrawn as being drawn to a non-elected invention.

Claim Objections

Claim 14 is objected to as being dependent upon a rejected base claim and reciting non-elected subject matter, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and deleting non-elected subject matter.

Response to Applicant's Arguments

Re: Claim Rejections - 35 USC § 103

Upon reconsideration, the rejection of claim 14 is withdrawn because it would not have been prima facie obvious to make the claimed antisense compound having SEQ ID No. 231. However this claim is objected to as stated above.

The rejection of claims 1, 5, 7-11, 16 and 59 under 35 U.S.C. 103(a) as being unpatentable over Stephenson et al. (BMC Molecular Biology 2001, Vol. 2, No. 15, pages 1-9), Bennett et al. (The Journal of Biological Chemistry, 1994, Vol. 268, No. 19, pages 14211-14218), Taylor et al. (DDT 1999, Vol. 4, No. 12, pages 562-567), Baracchini et al. (US Patent 5,801,154) and Tang et al. (Nucleic Acids Research 1993, Vol. 21, No. 11, pages 2729-2735) is maintained for the reasons of record.

New claims 92 and 93 recite claim limitations that have been deleted from independent claims 1 and 59 and therefore the rejection of record would still apply to these new claims.

With regard to claims 1, 5, 7-11, 16, 59, 92 and 93, Applicant's arguments filed 10/20/2008 have been fully considered but they are not persuasive. Applicant argues the Examiner has not satisfied the requirement of establishing a prima facie case of obviousness and emphasize the claimed EphB4 antisense compound is functionally defined by its ability to decrease expression of EphB4 in a cell. Applicant argues Stephenson et al. do not teach the use of antisense compounds let alone an antisense compound that decreases expression of EphB4 and the suggestion by Stephenson et

al. that "targeted disruption of the EphB4 gene" in colon cancer cells may provide useful information for developing strategies for treatment of colon cancer is entirely different from antisense technology. Applicant argues that the other cited references do not bridge the gap between the claimed invention and Stephenson et al. because they merely teach antisense technology in general and do not teach how to make or modify an antisense compound targeting and decreasing expression of an EphB4 gene.

In response to Applicants assertion that targeted disruption is different than antisense technology, while it is true that Stephenson et al. do not suggest the specific mechanism of antisense technology, the fact that Stephenson et al. found that EphB4 is overexpressed in colon cancer would lead one of ordinary skill in the art to seek methods of decreasing the expression of genes known to cause disease such as cancer. It was well known in the art at the time of the invention that antisense technology was a very effective method for decreasing the expression of genes. One of ordinary skill in the art would interpret the statement in Stephenson et al. to mean any disruption of the gene such that it would no longer function i.e. the gene would no longer express EphB4 given this gene was found to be overexpressed in colon cancer cells.

Antisense technology, while not defined as disruption of a gene in the instant specification or by Stephenson et al., is clearly known in the art to inhibit the function of a gene i.e. disrupt the gene such that the gene no longer expresses functional protein. It is unclear how Applicant can make the statement that the targeted disruption of the EphB4 gene described by Stephenson et al. is entirely different from antisense technology when Stephenson et al. has not provided a limiting definition of this process

to exclude antisense technology. Furthermore, it is unclear how Stephenson et al. can teach away from the claimed Invention when Stephenson et al. suggests disrupting the function of the gene to decrease the expression of said gene in an effort to provide treatment strategies to inhibit tumor cell growth and the claimed invention is drawn to an nucleic acid compound targeted to a EphB4 gene for the purpose of decreasing the expression of said gene. Therefore, one of ordinary skill in the art would take from Stephenson et al. that it would be beneficial in methods of treating colon cancer to inhibit the expression of EphB4 and would look to the teachings of the other cited references for guidance in making an antisense compound targeted to an EphB4 gene because antisense technology was well known in the art as an efficient method of inhibiting unwanted gene expression in cells.

Applicant's argument submitting that the skilled artisan would not have had a reasonable expectation of success even if these references were combined given that it was well known in the art that the activity of antisense oligonucleotides is unpredictable in cells is not convincing. Applicants point to support for this argument in the reference Summerton et al. included as Exhibit A in the response filed 10/20/2008 and conclude that because Summerton et al. recognized that antisense technology had many technical problems that may lead to inefficiency in cells, the use of any antisense compound is unpredictable in cells and therefore one of ordinary skill could not predict that the claimed antisense compound could be successfully made.

This line of reasoning is not convincing. First, Summerton et al. is a review article that gives an overview of new designs and structural properties that can be

incorporated into antisense compounds that solve the problem once recognized by first-generation antisense compounds. Nowhere in the reference is there a concluding statement that the use of antisense compounds is unpredictable in cells. What Summerton et al. does teach is that by incorporation of modified backbone and base moieties, antisense compounds have been improved to have high efficacy and specificity that makes them very promising therapeutics. The instant claims are drawn to such compounds comprising modified backbones or base moieties so Summerton et al. provides evidence that antisense compounds could predictably be made that would be capable of inhibiting gene expression in cells. Thus, contrary to Applicants assertion, the combination of references provide the skilled artisan with guidance and motivation to make an antisense compound targeted to an EphB4 gene wherein the compound would reasonably be expected to be capable of inhibiting the expression from an EphB4 gene.

As stated in the previous Office action and reiterated herein, one of ordinary skill in the art at the time of the invention would have wanted to create an antisense compound targeted to an EphB4 gene for the purpose of studying EphB4 function and whether inhibition of expression from this gene would be useful in the treatment of colon cancer given Stephenson et al. teach EphB4 is overexpressed in colon cancer cells. One of ordinary skill in the art would have wanted to provide the antisense oligonucleotide with increased stability by incorporation of modified nucleotides as taught by Baracchini et al. and would have wanted to protect the antisense compound from nuclease degradation by making the antisense double stranded as taught by Tang

et al. One would have expected to be able to create an antisense oligonucleotide sequence targeted to an EphB4 gene given that Taylor teaches that with software analysis and high affinity oligonucleotides, one of skill needs to screen only a few oligonucleotides to find one that inhibits its target 66-95%, and since Baracchini et al. teach making modified antisense compounds targeted to distinct regions of a target gene, the steps of making any antisense oligonucleotide are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Thursday between 6 and 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Examiner
Art Unit 1635